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Mixed Donor Chimerism after Allogeneic Transplant in Patients with Wiskott-Aldrich Syndrome

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Background: Wiskott-Aldrich syndrome (WAS) is a rare X-linked disorder characterized by a triad of immunodeficiency, eczema and thrombocytopenia. This is as a result of mutation in the WASP gene that regulates actin polymerization in hematopoietic cells. Currently, stem cell transplant (SCT) is the most reliable curative treatment with excellent results for patients with HLA-matched family or unrelated donors. However, mixed donor chimerism even in the setting of full myeloablative regimens is still a significant problem since mixed chimerism affecting the myeloid compartment may result in persistent thrombocytopenia. Thus, identifying factors associated with mixed donor chimerism after SCT in WAS patients is extremely important.

Methods: We performed a retrospective chart review of eleven children who underwent allogeneic transplant for WAS to identify any factors (i.e. pretransplant health of the patients, degree of thrombocytopenia, conditioning regimen, infection, peri-transplant factors, TH2 flare) that may be associated with mixed donor chimerism.

Results: The median age at transplant was 16 months (range 3-39) and the donor was MRD in 4, MUD in 5 and MMUD in 2. All patients received bone marrow apart from one who received cord. The mean WAS score was 2.7 (range 1-5) and diagnosis was confirmed by genetic testing in all patients. All were conditioned with myeloablative regimens. Nine received busulfan, cyclophosphamide, Ara-C or fludarabine and campath while 2 patients got busulfan, cyclophosphamide and ATG. The median nucleated cell dose from the marrow was 5.3 x 109/kg (range 3 to 7.9). The median times to neutrophil and platelet engraftment were 22.5 (range 13-27) and 19 (range 17-31) days respectively. The overall survival by Kaplan Meier analysis is 91%, 95%CI: 51%-99% at 2 year post transplant. Only one patient developed grade IV aGvHD and died on Day +99. Five of eleven (45%) had mixed donor chimerism, (range: 7-50%). Of these 5 patients, 2 had normalization of the platelet count despite the mixed chimerism, 2 had full donor chimerism after receiving a second transplant with the same donor, and 1 remains transfusion dependent awaiting a 2nd transplant. No statistically significant difference was found between WAS scores, donor type, conditioning, stem cell source, age at transplant and mixed chimerism amongst the eleven patients.

Conclusions: Although the overall survival of our patient population was excellent, it does not reflect a uniform result in terms of engraftment. None of our peri-transplant parameters are predictive of mixed chimerism or engraftment outcome. More correlative work is needed to assess genotype-phenotype risk factors for engraftment as well as pre transplant immunologic and disease states to better assess the risk of mixed chimerism and guide interventions to promote engraftment.

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Haploidentical Stem Cell Transplantation As a Therapeutic Option in Children with Previous Cord Blood Transplantation and Graft Failure. Successful Results in a Mexican Hospital

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Currently, in our environment, 50% of patients requiring transplantation cannot undergo this procedure due to lack of a donor.

Twenty patients with different pathologies Eleven patients had graft acceptance (55%) with complete chimerism. Nine (45%) patients had primary graft failure. Of the patients subjected to HT as rescue in case of cord graft failure, it was noted that 100% of the patients are alive after 40 months of follow-up with a statistically significant difference ($p = 0.02$) compared with those subjected to HT as the primary choice. This case review describes HT as a therapeutic tool in children without an available donor. Our objective was to describe the clinical features, complications and deaths in a series of children undergoing HT in the Instituto Nacional de Pediatria (INP) since 2009.

We included all patients undergoing HT between July 2009 and November 2012 .

Conditioning was done with fludarabine (30 mg/m^2) for 2 days, anti-thymocyte globulin (1.5 mg/kg/day) for 3 days, nodal radiotherapy (7 Gy) and melphalan (70 mg/m^2/day) for 2 days. For graft vs. host disease (GVHD) prophylaxis, cyclosporine (6 mg/kg/day) was used from day -1.

The method of CD34+ selection was contemplated for patients with immunodeficiency and CD3+ depletion for patients with oncology/hematology diseases.

For bivariate analysis of qualitative variables, c^{2}and Student t test were performed. OS and DFS curves were performed with the Kaplan-Meier method using SPSS v.20.0. Differences between the rates of OS or DFS based on cell dose, age, gender, and paternal or maternal donor were made using the log-rank test; $p<0.05$ was considered significant.

The median of cells infused was as follows: CD34+ 10.9 x 10^6/kg (range: 2 to 32 x 10^6/kg), CD3+ 14.2 x 10^5/kg and CD19+ 3.4 x 10^5/kg.

11 patients achieved graft (55%) with complete chimerism. Nine patients (45%) had primary graft failure. Of the 11 patients with complete chimerism, two patients had graft loss due to relapse of ALL (at 4 and 12 months post-HT). In a third case there was loss of the graft due to cytomegalovirus (CMV) at 21 months post-HT. Of the patients subjected to HT as rescue in case of cord graft failure, it was noted that 100% of the patients were alive at 40 months of follow-up with a